



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Postpartum Home Blood Pressure

Monitoring, Postpartum Treatment of Hypertensive Disorders of Pregnancy, and Peripartum Magnesium Sulfate Regimens for Preeclampsia With Severe Features

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for supplemental evidence and data submissions.

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on *Postpartum Home Blood Pressure Monitoring, Postpartum Treatment of Hypertensive Disorders of Pregnancy, and Peripartum Magnesium Sulfate Regimens for Preeclampsia With Severe Features*, which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:

E-mail submissions: epc@ahrq.hhs.gov

Print submissions:

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Center for Evidence and Practice Improvement

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ATTN: EPC SEADs Coordinator

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Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION: The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for *Postpartum Home Blood Pressure Monitoring, Postpartum Treatment of Hypertensive Disorders of Pregnancy, and Peripartum Magnesium Sulfate Regimens for Preeclampsia With Severe Features*. AHRQ is conducting this systematic review pursuant to Section 902 of the Public Health Service Act, 42 U.S.C. 299a.

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Postpartum Home Blood Pressure Monitoring, Postpartum Treatment of Hypertensive Disorders of Pregnancy, and Peripartum Magnesium Sulfate Regimens for Preeclampsia With Severe Features*, including those that describe adverse events. The entire research protocol is available online at:

<https://effectivehealthcare.ahrq.gov/products/hypertensive-disorders-pregnancy/protocol>

This is to notify the public that the EPC Program would find the following information on *Postpartum Home Blood Pressure Monitoring, Postpartum Treatment of Hypertensive Disorders of Pregnancy, and Peripartum Magnesium Sulfate Regimens for Preeclampsia With Severe Features* helpful:

- A list of completed studies that your organization has sponsored for this indication.

In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number.*

- *For completed studies that do not have results on ClinicalTrials.gov, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.*
- *A list of ongoing studies that your organization has sponsored for this indication. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.*
- *Description of whether the above studies constitute ALL Phase II and above clinical trials sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.*

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: <https://www.effectivehealthcare.ahrq.gov/email-updates>.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

Key Questions (KQ)

KQ 1: What are the effectiveness, comparative effectiveness, and harms of home blood pressure monitoring/telemonitoring in postpartum individuals?

KQ 2: What are the effectiveness, comparative effectiveness, and harms of pharmacological treatments for hypertensive disorders of pregnancy in postpartum individuals?

KQ 3: What are the comparative effectiveness and harms of alternative magnesium sulfate (MgSO₄) treatment regimens to treat preeclampsia with severe features during the peripartum period?

3.a. Are there harms associated with the concomitant use of particular antihypertensive medications during treatment with MgSO₄?

For **all Key Questions**, how do the findings vary by race, ethnicity, HDP subgroup, maternal age, parity, singleton/multiple pregnancies, mode of delivery, co-occurring conditions (e.g., obesity), and social determinants of health (e.g., postpartum insurance coverage, English proficiency, income, educational attainment)?

Contextual Question (CQ)

CQ 1: How are race, ethnicity, and social determinants of health related to disparities associated with incidence of HDP, detection, access to care, management, followup care, and clinical outcomes in individuals with postpartum hypertensive disorders of pregnancy?

Study Eligibility Criteria

Key Question 1 (Home BP Monitoring)

Population

- Postpartum individuals (with or without a prior HDP diagnosis)

Modifiers/Subgroups of interest

- Subgroups defined by ACOG HDP classification (some of which may arise *de novo* in the postpartum period)
 - chronic HTN
 - gestational HTN
 - preeclampsia (may be superimposed on chronic HTN)
 - preeclampsia with severe features (as defined by study authors)
 - *de novo* HTN postpartum
- Subgroups defined by BP diagnostic threshold(s)
- Race, ethnicity
- Maternal age, parity, singleton/multiple pregnancy, delivery (e.g., cesarean versus vaginal delivery, preterm versus term)
- Co-occurring disorders (e.g., obesity, diabetes)
- Subgroups defined by potential indicators of social determinants of health (e.g., insurance coverage, English proficiency, income, educational attainment)
- Access to technology (e.g., broadband internet, smartphone)

Interventions and intervention components

- Postpartum home BP monitoring interventions
 - Electronic, digital monitors, any

- With or without web-based connectivity and communication
- With or without education or training in use of monitor
- With or without validation of accuracy of patient's monitor
- *Exclude: Ambulatory BP monitoring (e.g., 24- or 48-hour continuous monitoring)*
- *Exclude: Monitors with manual inflation and auscultation*
- *Exclude: BP monitoring only by third parties, such as home health aides, visiting nurses*
- *Exclude: Very limited use of monitoring (e.g., single reading or single day)*
- *Exclude: Use of device only in laboratory or clinic setting*

Comparators

- No home BP monitoring (e.g., usual care with clinic-only BP monitoring)
- Alternative non-clinic-based BP monitoring approaches (e.g., kiosks, pharmacy-based BP monitoring, home health aide visits)
- Alternative education modalities about self-monitoring BP (e.g., demonstration of correct use, confirmation of appropriate cuff size)
- Alternative home BP monitor characteristics (e.g., direct transmission of results, prompts for communication of symptoms)
- Alternative home BP monitoring regimen (e.g., BP measurement frequency, duration)
- Alternative instructions for when to communicate results immediately (e.g., different BP threshold alerts)
- Alternative mode of communicating results (e.g., during clinic visit, automatic web-based, via text/email/portal/phone)
- Alternative clinician feedback processes
- No use of validation of accuracy of patient's monitor

Outcomes (prioritized outcomes have an asterisk and are in bold font)

- Blood pressure

- **Ascertainment of elevated BP or new onset HDP***
 - Time to clinical recognition of elevated BP
- **Treatment***
 - Initiation or discontinuation of antihypertensive medications
 - Increase or decrease in dose (or number) of antihypertensive medications
 - BP control (e.g., BP normalization)
- Documentation of BP after discharge
- Recognition of white coat HTN
- Severe maternal outcomes
 - **Maternal mortality, including pregnancy-related mortality***
 - **Severe maternal morbidity*** (e.g., **stroke***, eclampsia, pulmonary edema)
- Patient reported outcomes
 - Patient reported experience measures (PREMs) for example
 - **Satisfaction with postpartum care***
 - Ease of access to care
 - Quality of communication
 - Support to manage HTN
 - Patient Reported Experience Measure of Obstetric racism (PREM-OB Scale)
 - Patient reported outcome measures (PROMs), for example
 - **Global Quality of life***, e.g., SF-36
 - Psychosocial distress
 - **Anxiety***, e.g., State-Trait Anxiety Inventory (STAI)
 - **Depression***, e.g., Edinburgh Postnatal Depression Score (EPDS)
- Healthcare utilization
 - **Length of postpartum hospital stay***

- **Unplanned obstetrical triage area or clinic visits***
- **Emergency department visits***
- **Re-hospitalization after discharge***
- **Reduction of health disparities*** (increase in disparities included under *Harms*)
- Other Harms
 - **Generation or exacerbation of health disparities***
 - Anxiety associated with use of monitoring technology

Study Design

- Comparative studies (comparisons of different interventions or regimens)
 - Randomized controlled trials ($N \geq 10$ per group)
 - Nonrandomized comparative studies (prospective or retrospective) that use statistical techniques (e.g., regression adjustment, propensity score matching, inverse probability weighting) to reduce bias due to confounding)
- Any publication language (unless cannot be translated)
- Exclude
 - Single group (noncomparative) studies
 - Case-control studies
 - Claims database analyses
 - Feasibility studies
 - Device validation studies (not including validation of patients' monitors in the clinic)
 - Qualitative studies
 - Conference abstracts prior to 2020 (without subsequent, eligible peer-reviewed publication)

Timing

- Intervention: Day of birth through 1 year postpartum
 - Self-monitoring may start antenatal, in hospital, or postpartum, but must continue postpartum
- Outcomes: Any (postpartum)

Setting

- Outpatient postpartum management (although training and initiation may start in hospital or at clinic)
- Any publication date
- Any country

Key Question 2 (Treatment of HDP)

Population

- Postpartum individuals with diagnosed HDP (whether diagnosed antenatal, peripartum, or postpartum)

Modifiers/Subgroups of interest

- Subgroups defined by ACOG HDP classification (these may arise *de novo* in the postpartum period)
 - chronic HTN
 - gestational HTN
 - preeclampsia (may be superimposed on chronic HTN)
 - preeclampsia with severe features (as defined by study authors)
 - *de novo* HTN postpartum
- Subgroups defined by BP thresholds/categories
- Race, ethnicity

- Maternal age, parity, singleton/multiple pregnancy, mode of delivery (e.g., cesarean versus vaginal delivery, preterm versus term)
- Co-occurring disorders (e.g., obesity, diabetes)
- Subgroups defined by potential indicators of social determinants of health (e.g., insurance coverage, English proficiency, income, educational attainment)
- Use of home monitoring

Interventions

- Pharmacological treatments for HTN or HDP administered postpartum
 - Antihypertensive medications (single or combination therapies)
 - Loop diuretics (alone or in combination with antihypertensive medications)
- Exclude:
 - *Medication not available for use in the U.S.*
 - *Nonpharmacological treatments (e.g., uterine curettage)*
 - *Corticosteroids (e.g., for HELLP)*
 - *Interventions to prevent preeclampsia (e.g., low-dose aspirin)*
 - *Treatments not used to treat HDP (e.g., NSAIDs)*
 - *Behavioral modification (e.g., diet, exercise)*
 - *Non-medical interventions (e.g., traditional medicine, complementary and alternative medicine, meditation, mindfulness)*

Comparators

- Alternative specific treatments (e.g., alternative antihypertensive medication(s) or combinations of medications, alternative diuretic)
- Alternative treatment regimen (e.g., alternative dose, duration of treatment)
- Alternative blood pressure targets
- No treatment (or placebo)

- Exclude: *Excluded interventions*

Outcomes (prioritized outcomes have an asterisk and are in bold font)

- Intermediate outcomes
 - **Blood pressure control***
 - Measures of end-organ function
 - Cardiovascular measures (e.g., echocardiographic measurements of diastolic function and hypertrophy)
 - Kidney function (e.g., estimated glomerular filtration rate)
- Severe maternal outcomes
 - **Maternal mortality, including pregnancy-related mortality***
 - **Severe maternal morbidity*** (e.g., **stroke***, eclampsia, pulmonary edema)
- Patient reported outcomes
 - Patient reported experience measures (PREMs), for example
 - **Satisfaction with postpartum care***
 - Ease of access to care
 - Quality of communication
 - Support to manage HTN
 - Patient reported outcome measures (PROMs), for example
 - **Global Quality of life***, e.g., SF-36
 - Maternal-neonatal bonding, e.g., Postpartum Bonding Questionnaire
 - Psychosocial distress
 - **Anxiety***, e.g., State-Trait Anxiety Inventory (STAI)
 - **Depression***, e.g., Edinburgh Postnatal Depression Score (EPDS)
- Healthcare utilization
 - **Length of postpartum hospital stay***

- **Unplanned obstetrical triage area or clinic visits***
- **Emergency department visits***
- **Re-hospitalization after discharge***
- Infant health outcomes
 - **Breastfeeding outcomes (e.g., initiation, success, duration)***
- **Reduction of health disparities*** (increase in disparities included under *Harms*)
- Harms
 - **Severe adverse events*** (e.g., electrolyte abnormalities, severe hypotension)
 - **Infant morbidities*** (e.g., hypotension, other symptoms attributed to medication exposure via breast milk)
 - **Generation or exacerbation of health disparities***
 - Adverse interactions with other medications

Study Design

- Comparative studies (comparisons of different interventions or regimens)
 - Randomized controlled trials ($N \geq 10$ per group)
 - Nonrandomized comparative studies (prospective or retrospective) that use statistical techniques (e.g., regression adjustment, propensity score matching, inverse probability weighting) to reduce bias due to confounding
- Any publication language (unless cannot be translated)
- Exclude
 - Single group (noncomparative) studies
 - Case-control studies
 - Claims database analyses
 - Feasibility studies
 - Qualitative studies

- Conference abstracts prior to 2020 (without subsequent, eligible peer-reviewed publication)

Timing

- Intervention: Day of birth up to 1 year postpartum
 - Intervention may start antenatal, in hospital, or postpartum, but must continue postpartum
- Outcomes: Any (postpartum)

Setting

- Outpatient, non-acute management (treatment may start inpatient)
- Any publication date
- Any country

Key Question 3 (MgSO₄ for Preeclampsia with Severe Features)

Population

- Individuals who have preeclampsia with severe features (as defined by study authors) during the peripartum period (prior to and/or after delivery)
- *Exclude: Pregnant patients who are treated with MgSO₄ with the goal of suppressing premature labor, for fetal neuroprotection, or for other reasons*

Modifiers/Subgroups of interest

- Race, ethnicity
- Maternal age, parity, singleton/multiple pregnancy, mode of delivery (e.g., cesarean versus vaginal delivery, preterm versus term)
- Co-occurring disorders (e.g., obesity, diabetes)
- Subgroups defined by potential indicators of social determinants of health (e.g., insurance coverage, English proficiency, income, educational attainment)

- Timing of MgSO₄ administration or onset of preeclampsia with severe features with respect to delivery
 - Antepartum
 - Intrapartum
 - Postpartum
- Individuals with reduced kidney function

Interventions

- Peripartum MgSO₄ administration
 - Any dose, route (except oral), timing, duration of treatment, concomitant treatment, or regimen
- Exclude: Oral magnesium supplementation

Comparators

- Alternative MgSO₄ regimens
 - Different criteria for initiation of treatment
 - Different criteria for stopping (or continuing) treatment
 - Different criteria for altering dosing during treatment
 - Different loading dose
 - Different planned total dose
 - Different route
 - Different planned duration of treatment
 - Tailored interventions based on pharmacokinetic monitoring (i.e., based on serum Mg levels)
 - Combined treatment with antihypertensive medications (including regimens with alternative antihypertensive medications)
 - Other variations in regimens

- Exclude: No MgSO₄ treatment (either placebo, no treatment, or non-MgSO₄ comparators)
 - Except retain RCTs with placebo, no treatment, or non-MgSO₄ comparators and NRCSs comparing MgSO₄ with no MgSO₄ for postpartum preeclampsia with severe features

These may be included in network meta-analyses to indirectly compare alternative MgSO₄ regimens.

Outcomes (prioritized outcomes have an asterisk and are in bold font)

- Severe maternal health outcomes
 - **Maternal mortality, including pregnancy-related mortality***
 - **Severe maternal morbidity* (e.g., eclampsia*, stroke)**
- Newborn/child outcomes
 - **Infant morbidities*** (e.g., respiratory depression, Apgar score)
 - **Breastfeeding outcomes* (e.g., initiation, success, duration)**
 - Fetal/neonatal mortality
 - Cognitive function
- Healthcare utilization and functional status
 - Length of postpartum hospital stay
 - Time to ambulation
- Patient reported outcomes
 - Patient reported experience measures (PREMs) , for example
 - **Satisfaction with care***
 - Quality of communication
 - Support to manage preeclampsia treatment
 - Patient reported outcome measures (PROMs), for example
 - **Global Quality of life*, e.g., SF-36**

- **Specific to postpartum population***, e.g., Mother-Generated Index, Functional Status After Childbirth scales
- Psychosocial distress
 - **Anxiety***, e.g., State-Trait Anxiety Inventory (STAI)
 - **Depression***, e.g., Edinburgh Postnatal Depression Score (EPDS)
 - **Stress***, e.g., Impact of Event Scale
- **Maternal-neonatal bonding***, e.g., Postpartum Bonding Questionnaire
- **Reduction of health disparities*** (increase in disparities included under *Harms*)
- Maternal harms/adverse events
 - **Magnesium-related toxicity*** (respiratory depression, loss of reflexes, reduced urine output, need for calcium infusion)*
 - **Other clinically important adverse events*** (e.g., hypotension, neuromuscular blockade)
 - **Adverse drug interactions*** (e.g., with antihypertensive medications)
 - **Generation or exacerbation of health disparities***
 - Other serious (e.g., severe flushing)

Study Design

- Comparative studies (comparisons of different interventions)
 - Randomized controlled trials $N \geq 10$ per group
 - Comparisons between $MgSO_4$ and placebo/no treatment or non- $MgSO_4$ treatments must be randomized (for potential network meta-analyses)
 - Nonrandomized comparative studies (prospective or retrospective) that use statistical techniques (e.g., regression adjustment, propensity score matching, inverse probability weighting) to reduce bias due to confounding
- Any publication language (unless cannot be translated)

- Exclude
 - Single group (noncomparative) studies
 - Case-control studies
 - Claims database analyses
 - Feasibility studies
 - Qualitative studies
 - Conference abstracts prior to 2020 (without subsequent, eligible peer-reviewed publication)

Timing

- Intervention: Peripartum (antenatal, during delivery hospitalization, postpartum)
- Outcomes: Any

Setting

- Inpatient management
- Any publication date
- Any country

Dated: March 23, 2022.

Marquita Cullom,

Associate Director.